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Reply to the Editor:

We read with interest the comments addressed by Wurtz and coworkers on our article, ''Tracheal regeneration: Evidence of bone marrow stem cell involvement.''[1] We greatly appreciate their congratulations for having provided a ''convincing demonstration of bone marrow–derived stem cell migration to the grafted area after tracheal replacement with an aortic allograft in a New Zealand rabbit model.'' More generally, we thank them for their strong support to our pioneering experimental works,[2-5] which led to the first human applications.[6,7] Nevertheless, we would like to discuss some key points arising from their letter.

In our rabbit model, we observed a radically different evolution of the aortic graft. To answer precisely their comments, neither necrosis nor overdistention of the thoracic aorta by the endoprosthesis occurred in our experiments. A stent of 5 mm in diameter was inserted with moderate distention of the aorta so that the elastic tissue would not collapse. As shown in Figure 1 of the original article, stent and aortic dimensions matched well with the cervical tracheal diameter after graft interposition. Moreover, as underlined by our article, stent migration was one of the main complications, proving that the stenting has not been forcefully made. Perhaps age and weight of the rabbits in Wurtz and coworkers' experimentations were not properly chosen? We are also surprised by the polyethylene tube they reported using in their unpublished studies. In our sheep and human work, we paid great attention to base our studies on a tracheal prosthesis that had already been evaluated in clinical applications, and we decided to use a flexible pediatric tracheal silicone stent (Tracheobronxane Dumon; Novatech, La Ciotat, France).

Finally, did Wurtz and coworkers observe such necrosis both with and without stenting in their model? The real difference that we want to underline is the allotransplantation site of the aorta. Also, a muscle flap could be a better option than a fascial flap to promote revascularization. This has been clearly demonstrated in our experimental and clinical work on airway transplantation with aortic allografts.[7,8]

We completely agree with Wurtz and coworkers that ''the presence of bone marrow mesenchymal stem cells in the grafted area could result in their capacity for nonspecific migration and homing toward different kinds of damaged or injured tissues.'' As they have noted, we constructed our experimentations on the basis of mesenchymal stem cell circulating theory, hypothesizing that injured rabbits would use circulating mesenchymal stem cells to avoid bone marrow mobilization.[9] It is well known that unspecific mesenchymal stem cells migrate to inflammatory sites attracted by the liberation of chemokines on the place of injury. The real challenge is to find the other triggers orienting these cells to secondly differentiate to obtain tracheal regeneration.

We disagree with Wurtz and coworkers, however, who would compare these uncompleted results on the rabbit model with the first human applications, in which cartilage regeneration seems to be delayed. The structure of the human aorta is histologically closer to the aorta of the minipig than to the aorta of the rabbit. There is still hope to get similar results to those observed in these experimentations with cartilage regeneration. We are still working on multiple hypotheses to explain the delayed regeneration of human cartilage, such as patient age (older meaning no circulating growth factor), sex influence (more often men than women), tumoral pathology, previous impairing treatments (chemotherapy), and so on.

To conclude, the myth turned into reality with the first demonstration of tracheal regeneration in animal studies at the beginning of our experience.[2-4] Today, the main issue is to obtain the same regenerative processes in human beings. A prospective study (TRACHEOBRONC-ART trial) is in progress at our center to confirm not only the feasibility of airway transplantation with cryopreserved aortic allograft but also the possibility of airway regeneration in human beings.

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Notice of Correction

Re: Schaffer JM, Singh SK, Reitz BA, Oyer PE, Robbins RC, Mallidi HR. Heart transplant graft survival is improved after a reduction in panel reactive antibody activity. *J Thorac Cardiovasc Surg*. 2013;145:555-65.

In Figure 4 of the above-mentioned article, the 2 Kaplan-Meier curves were mislabeled: The curve for the patients who had a substantial panel reactive antibody reduction was labeled as the curve for patients who had a trivial panel reactive antibody reduction and vice versa. The corrected version of the figure is printed below.

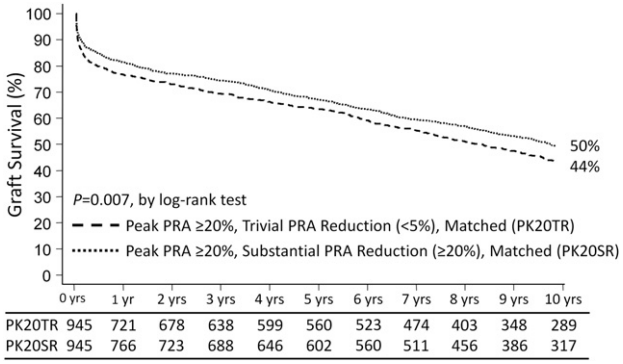

FIGURE 4. Kaplan–Meier estimate of graft survival after heart transplant in a propensity-matched cohort of patients with a peak PRA activity of 20% or more, stratified by whether a trivial or substantial reduction in PRA activity was achieved. *PRA*, Panel reactive antibody.